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TUKYSA Combination Significantly Improves Progression-Free Survival as First-Line Maintenance in HER2+ Metastatic Breast Cancer in HER2CLIMB-05 Trial

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NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced positive topline results from the Phase 3 HER2CLIMB-05 trial of first-line combination therapy with the tyrosine kinase inhibitor TUKYSA® (tucatinib) in patients with human epidermal growth factor receptor 2-positive (HER2+) metastatic breast cancer (MBC). HER2CLIMB-05 is evaluating TUKYSA versus placebo, both in combination with first-line standard-of-care maintenance therapy (trastuzumab plus pertuzumab) following chemotherapy-based induction. The trial met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in progression-free survival (PFS) by investigator assessment in the TUKYSA arm versus the placebo arm. Treatment with TUKYSA in combination with trastuzumab and pertuzumab was tolerable, with a safety profile generally consistent with the established safety profiles of each individual therapy.

“HER2+ breast cancer is a particularly challenging subtype, with many patients experiencing disease progression despite effective treatments in the first-line setting,” said Erika Hamilton, M.D., principal investigator of HER2CLIMB-05 and Director, Breast Cancer Research, Sarah Cannon Research Institute (SCRI). “The HER2CLIMB-05 results demonstrate that the addition of TUKYSA to first-line maintenance therapy may further lower the risk of disease progression or death, with a treatment that has a well-established safety profile.”

HER2 is overexpressed in up to 15-20% of breast cancers and is associated with poor prognosis, with an estimated five-year survival rate for HER2+ MBC of 41-47%, depending on HR status.[i,ii,iii] First-line standard of care maintenance treatment has remained unchanged since 2012, and the majority of HER2+ MBC patients face disease progression within two years of initiating therapy.[iv] Until recently, there have been limited advancements for these patients.

“Pfizer aims to help shape the future of front-line treatment for HER2+ MBC, where we see significant opportunity for a chemotherapy-free maintenance approach,” said Johanna Bendell, M.D., Chief Development Officer, Oncology, Pfizer. “The positive results from HER2CLIMB-05, combined with TUKYSA’s known safety profile in later-line settings, underscore its potential to play a meaningful role in front-line maintenance, where it may benefit a broader population of patients with HER2+ disease. We are grateful to the patients and investigators who contributed to this important research.”

Results from HER2CLIMB-05 will be presented at a future medical congress and discussed with regulatory authorities.

Since its initial approval in 2020, TUKYSA has become a standard of care for HER2+ MBC patients in the third-line setting and has been approved in more than 50 countries. In the United States, TUKYSA is approved by the U.S. Food and Drug Administration for use in combination with trastuzumab and capecitabine for adult patients with advanced unresectable or metastatic HER2+ breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting. TUKYSA is not currently approved for first-line treatment.

About the HER2CLIMB-05 Trial
HER2CLIMB-05 is a randomized, double blind, placebo-controlled, pivotal Phase 3 study evaluating the efficacy and safety of TUKYSA® (tucatinib) compared to placebo, both in combination with trastuzumab and pertuzumab, as maintenance therapy for patients with HER2+ metastatic breast cancer (MBC) following induction therapy in the first-line setting.

Study participants who completed induction therapy of trastuzumab, pertuzumab and a taxane with no evidence of progression were randomized to receive TUKYSA in combination with trastuzumab plus pertuzumab (n=326), or placebo in combination with trastuzumab plus pertuzumab (n=328). The primary endpoint is progression-free survival (PFS) as assessed by the investigator. Overall survival is a key secondary endpoint.

About TUKYSA® (tucatinib)
TUKYSA (tucatinib) is an orally administered tyrosine kinase inhibitor of HER2. TUKYSA is approved in combination with trastuzumab and capecitabine to treat adults with HER2-positive advanced unresectable or metastatic breast cancer, including patients with brain metastases who have received one or more prior anti-HER2 breast cancer treatments in the metastatic setting.

The full U.S. Prescribing Information for TUKYSA can be found here.

IMPORTANT TUKYSA® (tucatinib) SAFETY INFORMATION FROM THE U.S. PRESCRIBING INFORMATION

Warning and Precautions:

- **Diarrhea**: TUKYSA can cause severe diarrhea including dehydration, hypotension, acute kidney injury, and death. If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Based on the severity of the diarrhea, interrupt dose, then dose reduce or permanently discontinue TUKYSA.
  In HER2CLIMB, 81% of patients who received TUKYSA experienced diarrhea, including 0.5% with Grade 4 diarrhea and 12% with Grade 3 diarrhea. The median time to onset of the first episode of diarrhea was 12 days and the median time to resolution was 8 days. Diarrhea led to dose reductions of TUKYSA in 6% of patients and discontinuation of TUKYSA in 1% of patients. Prophylactic use of antidiarrheal treatment was not required on HER2CLIMB.
- **Hepatotoxicity**: TUKYSA can cause severe hepatotoxicity. Monitor ALT, AST, and bilirubin prior to starting TUKYSA, every 3 weeks during treatment, and as clinically indicated. Based on the severity of hepatotoxicity, interrupt dose, then dose reduce or permanently discontinue TUKYSA.
  In HER2CLIMB, 8% of patients who received TUKYSA had an ALT increase > 5 × ULN, 6% had an AST increase > 5 × ULN, and 1.5% had a bilirubin increase > 3 × ULN (Grade ?3). Hepatotoxicity led to dose reduction of TUKYSA in 8% of patients and discontinuation of TUKYSA in 1.5% of patients.
- **Embryo-fetal Toxicity**: TUKYSA can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TUKYSA and for 1 week after the last dose.

Adverse Reactions:
In HER2CLIMB, serious adverse reactions occurred in 26% of patients who received TUKYSA. Serious adverse reactions in ? 2% of patients who received TUKYSA were diarrhea (4%), vomiting (2.5%), nausea (2%), abdominal pain (2%), and seizure (2%). Fatal adverse reactions occurred in 2% of patients who received TUKYSA including sudden death, sepsis, dehydration, and cardiogenic shock. Adverse reactions leading to treatment discontinuation occurred in 6% of patients who received TUKYSA. Adverse reactions leading to treatment discontinuation of TUKYSA in ?1% of patients were hepatotoxicity (1.5%) and diarrhea (1%). Adverse reactions leading to dose reduction occurred in 21% of patients who received TUKYSA. Adverse reactions leading to dose reduction of TUKYSA in ?2% of patients were hepatotoxicity (8%) and diarrhea (6%). The most common adverse reactions in patients who received TUKYSA (?20%) were diarrhea, palmar-plantar erythrodysesthesia, nausea, hepatotoxicity, vomiting, stomatitis, decreased appetite, anemia, and rash.

Laboratory Abnormalities:
In HER2CLIMB, Grade ?3 laboratory abnormalities reported in ?5% of patients who received TUKYSA were decreased phosphate, increased ALT, decreased potassium, and increased AST. The mean increase in serum creatinine was 32% within the first 21 days of treatment with TUKYSA. The serum creatinine increases persisted throughout treatment and were reversible upon treatment completion. Consider alternative markers of renal function if persistent elevations in serum creatinine are observed.

About Pfizer Oncology
At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes three core mechanisms of action to attack cancer from multiple angles, including small molecules, antibody-drug conjugates (ADCs), and multispecific antibodies, including other immune-oncology biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, genitourinary cancer, hematology-oncology, and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to help people with cancer live better and longer lives.

About Pfizer: Breakthroughs That Change Patients' Lives
At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For 175 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on X at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Disclosure Notice
The information contained in this release is as of October 14, 2025. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer Oncology, TUKYSA® (tucatinib) and results from the Phase 3 HER2CLIMB-05 trial evaluating TUKYSA versus placebo, both in combination with first-line standard of care maintenance therapy (trastuzumab plus pertuzumab) in patients with HER2+ metastatic breast

cancer following chemotherapy-based induction, including their potential benefits and plans to present and discuss the HER2CLIMB-05 results with regulatory authorities, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of TUKYSA; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from the clinical studies; whether and when drug applications for TUKYSA may be filed in particular jurisdictions for any potential indications; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be pending or filed for TUKYSA, which will depend on a myriad of factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether TUKYSA for any potential indication will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety, and/or other matters that could affect the availability or commercial potential of TUKYSA; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments; any potential indication will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety, and/or other matters that could affect the availability or commercial potential of TUKYSA; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2024, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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[i]Tarantino P, et al. ESMO expert consensus statements (ECS) on the definition, diagnosis, and management of HER2-low breast cancer. *J An Onc*. 2023;34(8):645-659.

[ii]Wolff AC, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol. 2018;36(20):2105-2122.

[iii] National Cancer Institute. https://seer.cancer.gov/statfacts/html/breast-subtypes.html. Accessed October 8, 2025

[iv]Swain SM et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. Lancet Oncol. 2020;21(4):519-530.

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